Notice of Allowability	Application No.	Applicant(s)	
	09/644,387	AGOSTON ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio, Ph.D.	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.

2. ☒ The allowed claim(s) is/are *1-25*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 9/14/05
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit: 1617

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Robert Richards on November 16, 2005.

The application has been amended as follows:

Claim 14 has been rewritten as follows: --

14. A method for purifying 2-methoxyestradiol to a produce a 2-methoxyestradiol substantially free of steroid contaminants having estrogenic or carcinogenic effects and having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone comprising:

adding a solution comprising 2-methoxyestradiol to a chromatography medium; and

eluting the 2-methoxyestradiol off of the medium with a solvent system comprising a polar solvent and a non-polar solvent.

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Claims 16-20 have been rewritten as follows: --

16. A method for producing 2-methoxyestradiol substantially free of steroid contaminants having estrogenic or carcinogenic effects and having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone comprising:

protecting the 3- and I7-hydroxyl groups of estradiol;

reacting the protected estradiol with bromine and acetic acid to produce a 2-brominated derivative of estradiol;

reacting the 2-brominated derivative of estradiol with sodium methoxide in the presence of a copper catalyst;

removing the protecting groups on the 3- and I7-hydroxyl groups to produce 2-methoxyestradiol; and

purifying the 2-methoxyestradiol using liquid chromatography on an adsorption/partition medium with a solvent system comprising a polar and a nonpolar solvent.

17. A method for producing 2-methoxyestradiol substantially free of steroid contaminants having estrogenic or carcinogenic effects and having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone comprising:

ring-brominating estradiol by reacting estradiol with bromine in the presence of acetic acid to produce a ring-brominated intermediate;

reacting the ring-brominated intermediate with sodium methoxide in the present of a copper catalyst to produce 2-methoxyestradiol; and

purifying the 2-methoxyestradiol using liquid chromatography on an adsorption/partition medium with a solvent system comprising a polar and a nonpolar solvent.

18. A method for producing 2-methoxyestradiol substantially free of steroid contaminants having estrogenic or carcinogenic effects and having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone comprising:

protecting the 3- and l7-hydroxyl groups of estradiol;

reacting the protected estradiol with nitric acid and acetic acid to produce a 2-nitro derivative of estradiol;

reducing the 2-nitro derivative of estradiol to produce the corresponding 2-amino derivative of estradiol;

reacting the 2-amino derivative of estradiol under Sandmeyer conditions to produce a 3-,l7-hydroxyl protected 2-methoxyestradiol; and

removing the protecting groups on the 3- and l7-hydroxyl groups to produce 2-methoxyestradiol.

19. A method for producing 2-methoxyestradiol substantially free of steroid contaminants having estrogenic or carcinogenic effects and having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone comprising:

protecting the 3-hydroxyl group of estrone;

reacting the protected estrone with nitric acid and acetic acid to produce a 2-nitro derivative of estrone;

reducing the 2-nitro derivative of estrone to produce the corresponding 2-amino derivative of estrone;

reacting the 2-amino derivative of estrone under Sandmeyer conditions to produce a 3-hydroxyl protected 2-methoxyestrone;

removing the protecting group on the 3-hydroxyl group to produce 2-methoxyestrone; and

reducing the l7-keto group of 2-methoxyestrone to produce 2-methoxyestradiol.

20. A method for producing 2-methoxyestradiol substantially free of steroid contaminants having estrogenic or carcinogenic effects and having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone comprising:

brominating estradiol in the presence of acetic acid to produce a mixture of ring-brominated estradiols;

isolating 2-bromoestradiol from the mixture of estradiols; and

reacting the 2-bromoestradiol with sodium methoxide in the presence of a copper catalyst to produce 2-methoxyestradiol.

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Telephone Inquiry

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1617

BB
November 16, 2005